Physica D 239 (2010) 1567–1572

Contents lists available at ScienceDirect

Physica D

journal homepage: www.elsevier.com/locate/physd

On the equilibrium equation for a generalized biological membrane energy by using a shape optimization approach

A. Laadhari [a,b], C. Misbah [a,*], P. Saramito [b]

[a] Laboratoire de Spectrométrie Physique, 140 avenue de la physique, Université Joseph Fourier, and CNRS, 38402, Saint Martin d'Hères, France

[b] Laboratoire Jean Kuntzmann, Université Joseph Fourier and CNRS, B. P. 53, 38041 Grenoble Cedex 9, France

ARTICLE INFO

Article history:
Received 16 June 2009
Received in revised form
9 March 2010
Accepted 6 April 2010
Available online 11 May 2010
Communicated by M. Vergassola

Keywords:
Vesicle shape
Red cell membrane
Helfrich energy
Shape optimization

ABSTRACT

A mechanical equilibrium equation of a vesicle membrane under a generalized elastic bending energy is obtained in this paper. Moreover, the derivation of this equilibrium equation is based on some shape optimization tools. This approach is new and more concise than the tensorial tools used previously for this problem.

1. Introduction

Phospholipid membranes are abundant in biology. They represent the major component of the cytoplasmic membrane of real cells. They are also present within the cell cytoplasm (e.g. Golgi apparatus, a complex assembly of phospholipid layers which serve to form small vesicles for protein transport). Phospholipid membranes are also used in many industrial applications (e.g. giant liposome emulsions for cosmetics). Pure phospholipid vesicles (a closed membrane suspended in an aqueous solution) constitute an attractive model system in order to describe mechanical and viscoelastic behaviors of many cells, like red blood cells. They are also regarded as promising drug carriers for a delivery at specific sites in the organisms. This explains the increasing interest for biological membranes from various communities ranging from biology to applied mathematics. This contribution is concerned with a certain aspect of mathematical modeling of vesicles, or more generally of phospholipid membranes.

Vesicles are formed by amphiphilic molecules self-assembled in water to build bilayers, in a certain range of concentration and temperature. Several experimental and theoretical studies have focused on the configuration and equilibrium shapes of vesicles (for a review on equilibrium shapes see [1,2]), and on the effect of flow see a recent review [3]).

At room, as well as at the physiological temperature, the membrane is fluid (a two dimensional incompressible fluid). Due to incompressibility, the main mode of deformation of a vesicle is bending. A basic ingredient for biomembranes is thus bending energy. Helfrich [4] introduced a model in which the cost in bending energy is given by

$$\frac{k_c}{2}\int_\Gamma (H-H_0)^2\,\mathrm{d}s+\frac{k_g}{2}\int_\Gamma K\,\mathrm{d}s, \tag{1}$$

where $H = \kappa_1+\kappa_2$ is the mean curvature of the membrane surface, κ_1 and κ_2 are the principle curvatures, $K = \kappa_1\kappa_2$ is the Gauss curvature and H_0 represents the spontaneous curvature that describes the asymmetry effect of the membrane or its environment. The membrane surface is denoted by Γ while Ω represents the inside volume of the vesicle, such that $\Gamma = \partial\Omega$. The integrals are performed along the membrane surface where ds denotes a surface area, while, in this paper, dx will represent a volume element. The constants k_c and k_g have the dimension of an energy and represent the bending modulus and the Gaussian curvature modulus, respectively. The second term in the Helfrich model is a topological invariant by the virtue of the Gauss–Bonnet theorem that says if one is not interested in change of topology, then this contribution is a constant and can be ignored. We shall disregard in the energy the contribution coming from Gauss curvature, since we do not account for topological changes.

* Corresponding author. Tel.: +33 476514876; fax: +33 476514544.
E-mail addresses: Aymen.Laadhari@imag.fr (A. Laadhari), cmisbah@ujf-grenoble.fr (C. Misbah), Pierre.Saramito@imag.fr (P. Saramito).

0167-2789/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.physd.2010.04.001

The equilibrium shape of vesicle membranes is determined by minimizing the bending energy subject to two constraints: fixed volume (incompressible enclosed fluid) and fixed area (inextensible membrane). It is a shape optimization problem that writes in the saddle point formulation[1] where the Lagrangian[2] L is

$$L(\Omega;\sigma,p) = \int_\Gamma f(H)\,\mathrm{d}s + \sigma\left(\int_\Gamma \mathrm{d}s - A_0\right) + p\left(\int_\Omega \mathrm{d}x - V_0\right). \tag{2}$$

The scalars σ and p are Lagrange multipliers, and can be viewed as an effective surface tension and pressure difference, respectively. They enforce constant area A_0 and constant volume V_0 of the vesicle, respectively. The Helfrich energy has been generalized by introducing f, an arbitrary smooth function defined in $\mathbb{R}$. Notice that the classical case corresponds to the choice $f(H) = \frac{k_c}{2}(H - H_0)^2$.

The notion of saddle point can be intuitively understood as follows. We would like the energy to be minimal (or L to be minimal with respect to shape variation) and that at the same time L should behave with respect to σ and p in a such a way to be maximum, so that to enforce constant volume and area (i.e. to suppress the terms proportional to σ and p in L).

Since L is differentiable, any saddle-point $(\Omega;\sigma,p)$ of L satisfies three conditions:

$$\frac{\partial L}{\partial \Omega}(\Omega;\sigma,p) = 0, \qquad \frac{\partial L}{\partial \sigma}(\Omega;\sigma,p) = 0 \quad \text{and} \quad \frac{\partial L}{\partial p}(\Omega;\sigma,p) = 0. \tag{3}$$

The two last conditions leads directly to the area and volume constraints, respectively. Thus looking for zeros of derivatives with respect to Lagrange multipliers is equivalent to imposing the two constraints. The aim of this paper is to show that the first condition, that involves the shape derivative $\partial/\partial\Omega$, leads to:

$$p + \sigma H + f(H)H + (2K - H^2)f'(H) - \Delta_s(f'(H)) = 0. \tag{4}$$

Notice that the choice $f(H) = \frac{k_c}{2}(H - H_0)^2$ leads to the classical equilibrium condition:

$$p + \sigma H + k_c\left(\frac{1}{2}(H - H_0)[4K - H(H + H_0)] - \Delta_s H\right) = 0 \tag{5}$$

where Δ_s is the surface Laplacian (known also as the Laplace–Beltrami operator), and will be defined explicitly in this paper. The result (5) was first derived in [4], relation (31). Notice that these authors used the same notation H for $-(\kappa_1 + \kappa_2)/2$, i.e. minus half of the present definition of the mean curvature $H = \kappa_1 + \kappa_2$. In that paper use of several concepts of differential geometry were evoked (first and second fundamental forms) in order to arrive to the final result. Similar concepts were used (in a somewhat more general manner by using quite involved knowledge in differential geometry like the Gauss–Godazzi–Mainardi and Gauss–Weingarten equations) in Ref. [5] in order to derive the shape equation. The calculation was exemplified for the Helfrich energy and extended to a functional of the form H^n (where n is any integer).

The main objective of this paper is to provide a derivation which is concise and self-contained. Our derivation uses quite simple and classical notions. While we will, in passing, quote some known expressions and Lemma in the mathematical literature, we shall provide their direct derivation here. Our derivation can be made general without specifying the functional expression $f(H)$. We shall discuss in the conclusion when generalized functionals can be expected to arise.

The paper is organized as follow: the second section introduces some notations and preliminary results while the third one aim at obtaining the equilibrium condition for the generalized expression (2) of the Helfrich energy. The paper is completed by a mathematical Appendix.

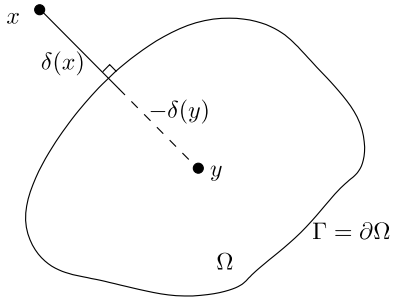

Fig. 1. Schematic view of the geometry. δ, the distance function, is positive for x outside Ω and negative inside. This is the signed distance.

2. Notations and preliminary results

All surface operators used in this paper are defined here. Let $\mathbf{n}$ denotes the unit outward normal vector to the shape Ω. Let f be any scalar function and $\mathbf{v}$ be any vector field. The surface gradient, the surface divergence and the Laplace–Beltrami operator are respectively expressed by:

$$\nabla_s f = (\mathbf{I} - \mathbf{n}\otimes\mathbf{n})\nabla f = \nabla f - (\mathbf{n}.\nabla f)\mathbf{n}, \tag{6}$$

$$\nabla_s.\mathbf{v} = (\mathbf{I} - \mathbf{n}\otimes\mathbf{n}) : \nabla\mathbf{v} = \nabla.\mathbf{v} - ((\nabla\mathbf{v}).\mathbf{n}).\mathbf{n}, \tag{7}$$

$$\Delta_s f = \nabla_s.(\nabla_s f). \tag{8}$$

The boundary Γ is then parametrized by a level set function δ, defined, for all $x \in \mathbb{R}^3$, as a signed distance (see Fig. 1):

$$\delta(x) = \begin{cases} \inf\limits_{y\in\Gamma} |y - x| & \text{when } x \notin \Omega, \\ -\inf\limits_{y\in\Gamma} |y - x| & \text{otherwise.} \end{cases}$$

Then, the normal expresses as a gradient: $\mathbf{n} = \nabla\delta$ (since $|\nabla\delta| = 1$).

Let us now express the mean and the Gauss curvatures. Let $A = \nabla_s\mathbf{n}$. Its characteristic polynom writes:

$$\mathcal{P}_A(\lambda) = \det(A - \lambda\mathbf{I}) = -\lambda^3 + I_1\lambda^2 - I_2\lambda + \det(A),$$

where $I_1 = A_{ii}$ and $I_2 = (A_{ii}A_{jj} - A_{ij}A_{ji})/2$ (repeated indices convention is used), are two invariants; see below.

Let us first show that $A = \nabla_s\mathbf{n} = \nabla\mathbf{n}$. From the definition (6) of ∇_s, it is equivalent to show that $\mathbf{n}.\nabla\mathbf{n} = 0$. On the one hand, since $|\mathbf{n}|^2 = 1$, we have $\nabla(\mathbf{n}.\mathbf{n}) = 0$. On the other hand, by expansion we have $\nabla(\mathbf{n}.\mathbf{n}) = 2(\mathbf{n}.\nabla)\mathbf{n} + 2\mathbf{n}\wedge\mathbf{rot}(\mathbf{n})$. Then $(\mathbf{n}.\nabla)\mathbf{n} = -2\mathbf{n}\wedge\mathbf{rot}(\mathbf{n})$. Next, since $\mathbf{n} = \nabla\delta$, we have $\mathbf{rot}(\mathbf{n}) = \mathbf{rot}(\nabla\delta) = 0$. Finally $\mathbf{n}.\nabla\mathbf{n} = 0$ and then $A = \nabla\mathbf{n}$.

Moreover, from definition of A, it is also the Hessian of the level set function: $A = (\nabla\otimes\nabla)\delta$. Thus A is symmetric and admits three *real* eigenvalues. Since $\mathbf{n}.\nabla\mathbf{n} = \mathbf{n}.A = 0$, A has a zero eigenvalue, associated to the eigenvector $\mathbf{n}$. Let us denote κ_1, κ_2 the two others eigenvalues of A. There exists an orthonormal eigenvector system $(\mathbf{e}_1, \mathbf{e}_2, \mathbf{n})$ associated to $(\kappa_1, \kappa_2, 0)$ such that $A = \kappa_1\mathbf{e}_1\otimes\mathbf{e}_1 + \kappa_2\mathbf{e}_2\otimes\mathbf{e}_2$. By definition [6, p. 47], the values κ_1 and κ_2 are called the principle curvatures and the vectors $\mathbf{e}_1$ and $\mathbf{e}_2$, the principle directions of curvature. The mean curvature

[1] For a mathematical point of view, the saddle point problem is written as: find (Ω,σ,p) such that

$$\inf_{\Omega\subset\mathbb{R}^3}\sup_{\sigma,p\in\mathbb{R}} L(\Omega;\sigma,p).$$

[2] Splitting the couple of variables (σ,p) from the variable Ω is a customary rule in mathematical literature in order to emphasize the fact that the two set of variable have different roles.

and the Gauss curvature are, by definition $H = \kappa_1 + \kappa_2$ and $K = \kappa_1\kappa_2$, respectively. Notice that as coefficients of the characteristic polynom, they are invariant by any change of basis, and thus in the eigensystem we find: $I_1 = H$ and $I_2 = K$. Going back to the definition of I_1 and I_2 in terms of $A = \nabla\mathbf{n}$ leads to the following expression of the mean and the Gauss curvatures:

$$H = \nabla_s.\mathbf{n} = \nabla.\mathbf{n} \quad \text{and} \quad 2K = H^2 - \nabla\mathbf{n} : \nabla\mathbf{n}^T. \tag{9}$$

Notice that the use of the level set function δ enables us to extend the quantities $\mathbf{n}$, H and K in the whole $\mathbb{R}^3$ space while their original definitions was introduced only on the surface Γ.

3. Obtaining the equilibrium equation

For any sufficiently regular shape deformation $\mathbf{u}$, we denote $\Omega_\mathbf{u} = (\mathbf{I} + \mathbf{u})(\Omega) = \{x + \mathbf{u}(x) \in \mathbb{R}^3; x \in \Omega\}$ the deformed shape (see Fig. 2).

Let us denote by $E(\Omega)$, $A(\Omega, \sigma)$ and $V(\Omega, p)$ the first, second and third terms of the right-hand side in (2), respectively. From Lemma A.1 derived in Appendix A, we get:

$$\frac{\partial V}{\partial \Omega}(\Omega, p)(\mathbf{u}) = p \int_\Gamma \mathbf{u}.\mathbf{n}\, ds. \tag{10}$$

Again, from Lemma A.1:

$$\frac{\partial A}{\partial \Omega}(\Omega, \sigma)(\mathbf{u}) = \sigma \int_\Gamma H\, \mathbf{u}.\mathbf{n}\, ds. \tag{11}$$

The rest of the paragraph deals with the $E(\Omega)$ term. From Lemma A.2 derived in the Appendix, we obtain:

$$\frac{\partial E}{\partial \Omega}(\Omega)(\mathbf{u}) = \int_\Gamma \frac{\partial f(H)}{\partial \Omega}(\Omega)(\mathbf{u})\, ds + \int_\Gamma \left(f(H)(\Omega)\, H + \frac{\partial\,(f(H))\,(\Omega)}{\partial \mathbf{n}} \right) \mathbf{u}.\mathbf{n}\, ds, \tag{12}$$

where $\partial/\partial\mathbf{n} = \mathbf{n}.\nabla$ denotes the directional (or normal) derivative. The normal $\mathbf{n}$, which also depends on the shape Ω is differentiable and its shape derivative in any direction $\mathbf{u}$ writes [7]: $\frac{\partial \mathbf{n}}{\partial \Omega}(\Omega)(\mathbf{u}) = -\nabla_s(\mathbf{u}.\mathbf{n})$. This expression can be derived by considering a particular elementary local displacement $\mathbf{u} = \mathbf{v}dt$ of the interface Γ, where $\mathbf{v}$ is the velocity. Recall that the level set function satisfies at each time $\delta(t, x(t)) = 0$, so that $\delta(t + dt, x(t + dt)) = 0$, and the difference of δ between $t + dt$ and t divided by dt (which defines the material derivative D/Dt) is also zero, and this yields (upon a Taylor expansion with respect to dt)

$$\frac{D\delta}{Dt} = \frac{d\delta}{dt} + \mathbf{v}.\nabla\delta = 0.$$

Then we get the following expression for $d\delta$ (upon multiplication of the above equation by dt on both sides) of the level set function:

$$d\delta = -\nabla\delta.\mathbf{u} \tag{13}$$

where $d\delta$ represents an elementary local displacement of the shape.

The shape derivative of the normal is given by the Fréchet differentiation of $\mathbf{n} = \frac{\nabla\delta(x)}{|\nabla\delta(x)|}$, in the direction $d\delta$, since the propriety $|\nabla\delta(x)| = 1$ for all position x in $\mathbb{R}^3$ is not preserved if the displacement $d\delta$ is applied. Consequently, using (13), the shape derivative (see also foot note for the shape derivative along direction $\mathbf{u}$) of $\mathbf{n} = \frac{\nabla\delta(x)}{|\nabla\delta(x)|}$ is given by

$$\frac{\partial \mathbf{n}}{\partial \Omega}(\Omega)(\mathbf{u}) = \lim_{\varepsilon \to 0} \frac{\mathbf{n}(\delta + \varepsilon d\delta) - \mathbf{n}(\delta)}{\varepsilon} = \frac{\nabla(-\mathbf{u}.\nabla\delta)}{|\nabla\delta|} - \frac{[\nabla(-\mathbf{u}.\nabla\delta).\nabla\delta]\,\nabla\delta}{|\nabla\delta|^3}. \tag{14}$$

By considering the elementary local displacement $d\delta$, we have $|\nabla\delta(x)| \to 1$ when $\varepsilon \to 0$, and hence

$$\frac{\partial \mathbf{n}}{\partial \Omega}(\Omega)(\mathbf{u}) = -\nabla(\mathbf{u}.\mathbf{n}) + [\mathbf{n}.\nabla(\mathbf{u}.\mathbf{n})]\mathbf{n}.$$

Then,

$$\frac{\partial \mathbf{n}}{\partial \Omega}(\Omega)(\mathbf{u}) = -\nabla_s(\mathbf{u}.\mathbf{n}). \tag{15}$$

This result can be shown otherwise (see [8, eq. A7]) by following a phase-field approach. Note at this point that an interesting derivation of the final result (4) has been given recently [9,10] without taking the limit $|\nabla\delta(x)| \to 1$. In [8] (see their Appendix A) only the Helfrich energy was considered and not the generalized one, as done in [9,10]. The same type of derivation as the phase field one has been given by using a level set approach [11]. Finally, another work is worth of mention [12] where a thermodynamical consistent derivation of a phase field approach arrived to the same conclusion.

From $H = \nabla.\mathbf{n}$, we obtain $\frac{\partial H}{\partial \Omega}(\Omega)(\mathbf{u}) = -\nabla.[\nabla_s(\mathbf{u}.\mathbf{n}(\Omega))]$ and then:

$$\frac{\partial f(H)}{\partial \Omega}(\Omega)(\mathbf{u}) = f'(H)\, \frac{\partial H}{\partial \Omega}(\Omega)(\mathbf{u}) = -f'(\nabla.\mathbf{n})\, \nabla.[\nabla_s(\mathbf{u}.\mathbf{n})].$$

Next, (12) leads to:

$$\frac{\partial E}{\partial \Omega}(\Omega)(\mathbf{u}) = \int_\Gamma f(H)(\Omega)\, H\, \mathbf{u}.\mathbf{n}\, ds + \int_\Gamma f'(H)\, \frac{\partial H}{\partial \mathbf{n}}\, \mathbf{u}.\mathbf{n}\, ds - \int_\Gamma f'(H)\, \nabla.[\nabla_s(\mathbf{u}.\mathbf{n})]\, ds. \tag{16}$$

Let us denote by T the last term of the right-hand side. Then,

$$T = -\int_\Gamma f'(H)\, \nabla.(\nabla_s(\mathbf{u}.\mathbf{n}))\, ds = \int_\Gamma \nabla_s(\mathbf{u}.\mathbf{n}).\nabla(f'(H))\, ds - \int_\Gamma \nabla.\left(f'(H)\nabla_s(\mathbf{u}.\mathbf{n})\right) ds. \tag{17}$$

• **Simplification 1**. Recall that, for any tangential vector field $\mathbf{v_T}$, the Stokes theorem over the closed surface Γ yields

$$\int_\Gamma \nabla_s.\mathbf{v_T}\, ds = 0. \tag{18}$$

We chose $\mathbf{v_T} = f'(H)\nabla_s(\mathbf{u}.\mathbf{n})$. By (7) and (18), we have

$$\int_\Gamma \nabla.\mathbf{v_T}\, ds - \int_\Gamma (\nabla\mathbf{v_T}.\mathbf{n})\, .\mathbf{n}\, ds = 0. \tag{19}$$

Using the summation of repeated indices convention, we have:

$$(\nabla\mathbf{v_T}.\mathbf{n})\, .\mathbf{n} = \mathbf{n}_i\mathbf{n}_j\partial_j\mathbf{v_T}_i = \mathbf{n}_j\partial_j(\mathbf{n}_i\mathbf{v_T}_i) - \mathbf{v_T}_i\mathbf{n}_j\partial_j\mathbf{n}_i.$$

Since $\mathbf{n}.\nabla\mathbf{n} = 0$ (see Section 2) we get:

$$(\nabla\mathbf{v_T}.\mathbf{n})\, .\mathbf{n} = \mathbf{n}.\nabla(\mathbf{n}.\mathbf{v_T}) - \mathbf{v_T}.[(\mathbf{n}.\nabla)\mathbf{n}] = 0.$$

Consequently,

$$\int_\Gamma \nabla.\left(f'(H)\nabla_s(\mathbf{u}.\mathbf{n})\right) ds = 0. \tag{20}$$

Recall that, for any scalar function g and any vector field $\mathbf{v}$ defined over the closed surface Γ, we have the following identity (see Appendix C):

$$\int_\Gamma \nabla_s g.\mathbf{v}\, ds = -\int_\Gamma g\, \nabla_s.\mathbf{v}\, ds + \int_\Gamma g\, \mathbf{v}.\mathbf{n}\, H\, ds.$$

With $g = \mathbf{u}.\mathbf{n}$ and $\mathbf{v} = \nabla(f'(H))$, using (20), we get:

$$T = -\int_\Gamma \nabla_s.\left(\nabla(f'(H))\right) \mathbf{u}.\mathbf{n}\, ds + \int_\Gamma \frac{\partial(f'(H))}{\partial \mathbf{n}}\, H\, \mathbf{u}.\mathbf{n}\, ds. \tag{21}$$

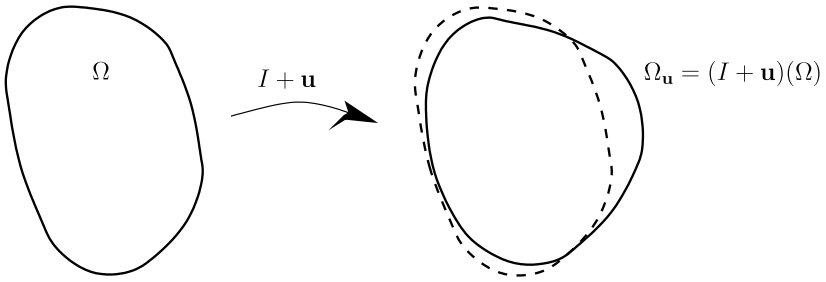

Fig. 2. Representation of the deformed domain $\Omega_{\mathbf{u}} = (\mathbf{I}+\mathbf{u})(\Omega)$.

Then (16) becomes:

$$\frac{\partial E}{\partial \Omega}(\Omega)(\mathbf{u}) = \int_\Gamma \left(f(H)\, H + f'(H)\, \frac{\partial H}{\partial \mathbf{n}} + \frac{\partial (f'(H))}{\partial \mathbf{n}}\, H - \nabla_s . \left[\nabla (f'(H)) \right] \right) \mathbf{u}.\mathbf{n}\, \mathrm{d}s. \tag{22}$$

This completes our derivation, in principle. However, some useful simplifications can be made, as shown below.

• **Simplification 2**. Using the summation of repeated indices convention, we have:

$$\frac{\partial H}{\partial \mathbf{n}} = \mathbf{n}.\nabla\left(\nabla.\mathbf{n}\right) = \mathbf{n}_i \partial_i \partial_j \mathbf{n}_j = \partial_j \left(\mathbf{n}_i \partial_i \mathbf{n}_j \right) - \partial_i \mathbf{n}_j \partial_j \mathbf{n}_i$$
$$= \nabla . \left((\mathbf{n}.\nabla)\, \mathbf{n} \right) - \nabla \mathbf{n} : \nabla \mathbf{n}^T .$$

Next, using expression (9) of the Gauss curvature K, we obtain:

$$\frac{\partial H}{\partial \mathbf{n}} = 2K - H^2 + \nabla . \left[(\mathbf{n}.\nabla)\, \mathbf{n} \right].$$

Finally, since $\mathbf{n}.\nabla \mathbf{n} = 0$ (see Section 2) we get:

$$\frac{\partial H}{\partial \mathbf{n}} = 2K - H^2. \tag{23}$$

• **Simplification 3**. From (6) we have:

$$-\nabla_s . \left\{ \nabla (f'(H)) \right\} = -\nabla_s . \left\{ \nabla_s (f'(H)) + \left(\mathbf{n}.\nabla (f'(H)) \right) \mathbf{n} \right\}$$
$$= -\Delta_s (f'(H)) - (\mathbf{n}.\nabla_s) \left\{ \mathbf{n}.\nabla (f'(H)) \right\} - (\mathbf{n}.\nabla)(f'(H))\, (\nabla.\mathbf{n}).$$

Notice that, from definition (6) of ∇_s, we have $\mathbf{n}.\nabla_s = 0$ and then:

$$-\nabla_s . (\nabla (f'(H))) = -\Delta_s (f'(H)) - \frac{\partial (f'(H))}{\partial \mathbf{n}}\, H. \tag{24}$$

Using the two simplifications (23) and (24), relation (22) becomes:

$$\frac{\partial E}{\partial \Omega}(\Omega)(\mathbf{u}) = \int_\Gamma \left\{ f(H)\, H + f'(H)\, (2K - H^2) - \Delta_s (f'(H)) \right\} \mathbf{u}.\mathbf{n}\, \mathrm{d}s.$$

Finally, using relation (10), (11), the previous relation leads to:

$$\frac{\partial L}{\partial \Omega}(\Omega; \sigma, p)(\mathbf{u}) = \int_\Gamma \left\{ f(H)\, H + f'(H)\, (2K - H^2) - \Delta_s (f'(H)) + p + \sigma\, H \right\} \mathbf{u}.\mathbf{n}\, \mathrm{d}s. \tag{25}$$

This last expression leads directly to the equilibrium condition (4).

4. Conclusion and discussion

We have provided a new and self-contained derivation of the force for a biological membrane. We have extended the derivation to a generalized expression of the functional $f(H)$. The Helfrich energy can be motivated by assuming that the stretching energy is of harmonic type (the energy is proportional to the square of change of distance from a certain configuration). In more complex situations, like red blood cells for example, this assumption is not obvious, in that a nonlinear constitutive law may constitute a better approximation. We must make a clear distinction between the bending modes and the in-plane shear modes. Bending modes arise both for vesicles and RBCs. When their membrane is bent this implies a small stretching of the membrane (say a change in the natural distance between molecules). For simplicity, consider a small infinitesimal portion of the membrane in two dimensions (the membrane is a line). The membrane has a width ϵ (distance between the internal and external layer of the membrane). The change in distance of that portion costs an energy (per unit area) $k_1(\ell_1 - \ell_{10})^2/2 + k_2(\ell_1 - \ell_{10})^2/2$ (harmonic approximation) were k_1 and k_2 are "spring" constants (per unit area) of the internal and external layers of the membrane, ℓ_1 and ℓ_2 are the actual length of the external and internal portion of the membrane, and ℓ_{10} and ℓ_{20} their natural equilibrium lengths. It is then a simple matter to show [13,2] that this energy can be rewritten as $\kappa(H - H_0)^2/2$ with $\kappa = (k_1 + k_2)(\ell\epsilon/2)^2$ where ℓ is the natural length of the neutral surface. It is then clear that the Helfrich energy follows from the local (i.e. at a given local region of the membrane) harmonic approximation. This type of reasoning is appropriate for pure vesicle membranes. In a more complex situations as is the case probably with a RBCs, and with other entities or tissues where the local constitutive law is not harmonic, the harmonic approximation may attain its limit of validity. For example if bending is limited by stretching of the cytoskeleton, or by a complex network the energy can exhibit non harmonic effects. In a network with macromolecules often entropic contribution of stretching of the network is important. In that case the force is a nonlinear function of change of distances (the energy is not harmonic) [14]. In that case, following the above type of analysis the effective bending energy will also exhibit terms which are not quadratic in H, which is the situation treated here.

The bending force is obtained upon variation of the effective energy with respect to shape, the topic of the present paper. Of course, in addition to bending modes, shear modes in the planes can be excited, and the bending energy must be supplemented with the corresponding contributions. The full force would be the sum of the force derived here plus a shear force arising from the variation of the energy with respect to the two variables representing the membrane in-plane displacement.

Another, perhaps more frequent, situation is that where macromolecules (like proteins) interact with a membrane [15]. The Helfrich energy $k_c/2 \int_\Gamma (H - H_0)^2 \mathrm{d}s$ should be supplemented with a term of the form $\int_\Gamma F(c)$ where F is certain function of protein concentration. In addition, H_0 (the spontaneous curvature) is generally a c-dependent function (see [15]). The total energy takes the form

$$J = \frac{k_c}{2} \int_\Gamma (H - H_0)^2 \mathrm{d}s + \int_\Gamma F(c) \mathrm{d}s. \tag{26}$$

Minimisation of the full energy with respect to c leads to

$$F'(c) - k_c (H - H_0) H_0'(c) = 0. \tag{27}$$

Solving for c yields, generically a nonlinear relation between c and H, and reporting the result into the original energy amounts to minimizing a generalized functional of the form $\int_\Gamma f(H)$, that is an expression of the form dealt with in this paper.

Suppose, as a way of example, that F is a quadratic function of c, $F = \alpha(c - c_0)^2/2$, where c_0 is some natural equilibrium concentration in the absence of coupling with bending modes and α is a positive parameter. Consider, in order to fix idea, the case where H_0 is a linear function of c, $H_0 = S_0(1 + \beta c)$, where S_0 is the natural spontaneous curvature in the absence of adsorbed molecules. From Eq. (27) one gets $c = a + bH$ with $a = c_0 - k_c S_0^2 \beta(1 + \beta c_0)/[\alpha + k_c(\beta S_0)^2]$ and $b = k_c S_0 \beta/[\alpha + k_c(\beta S_0)^2]$. Reporting into the energy (26) one obtains an effective energy (up to an additive constant, which is unimportant for our purposes) given by

$$J = \frac{\bar{k}_c}{2} \int_\Gamma (H - \bar{S}_0)^2 \mathrm{d}s \tag{28}$$

where the energy has the form of the Helfrich one with renormalized bending modulus and spontaneous curvature given by $\bar{k}_c = k_c(1 - S_0\beta b)^2 + \alpha b^2 > 0$ and $\bar{S}_0 = [\alpha b^2 S_0(1 + \beta c_0) + k_c S_0(1 + \beta a)(1 - S_0\beta b)]/\bar{k}_c$. This agrees with the result of Leibler [13]. The situation is different for more general functions $F(c)$. Typical examples are found in the study in biological membranes coupled with a concentration field (see [16] and references therein), where the functional $F(c)$ contains cubic and quartic terms in c. If the dependence with c were not quadratic (say if it contains quartic terms or terms of higher order) then by repeating the above example we would then have an effective energy (after elimination of c) that has the form $\int_\Gamma f(H)$. The derivation presented here can then be used to determine the effective bending force.

Acknowledgements

The authors acknowledge the financial support from ANR (Agence National de la Recherche), project MOSICOB. C.M. is grateful to CNES (Centre National d'Etudes Spatiales) for the financial support.

Appendix A. Some shape optimization tools

The notion and basic tools of shape derivative [17,7,18] is recalled in this Appendix. Starting from a smooth reference open set Ω, with boundary $\Gamma = \partial\Omega$, we consider domains of the type $\Omega_{\mathbf{u}} = (\mathbf{I} + \mathbf{u})(\Omega)$ (see Fig. 2) with $\mathbf{I}$ denotes the identity in $\mathbb{R}^3$ and $\mathbf{u}$ is any sufficiently regular vector field.

Definition A.1. The shape derivative of $J(\Omega)$ versus Ω is defined as the Fréchet derivative at $\mathbf{u} = 0$ of $\mathbf{u} \to J((\mathbf{I} + \mathbf{u})(\Omega))$, i.e.[3]

$$J((\mathbf{I} + \mathbf{u})(\Omega)) = J(\Omega) + \frac{\partial J}{\partial \Omega}(\Omega)(\mathbf{u}) + o(\mathbf{u})$$
$$\text{with } \lim_{\mathbf{u}\to 0} \frac{\|o(\mathbf{u})\|}{\|\mathbf{u}\|} = 0,$$

where $\frac{\partial J}{\partial \Omega}(\Omega)(\mathbf{u})$ is linear and continuous with respect to $\mathbf{u}$ and where $\|.\|$ denotes the usual Euclidean norm in $\mathbb{R}^3$.

Lemma A.1. *Considering a smooth bounded open set $\Omega \in \mathbb{R}^3$ and $f(x)$ a smooth function defined in $\mathbb{R}^3$. Define*

$$J_{vol}(\Omega) = \int_\Omega f(x)\,\mathrm{d}x \quad \text{and} \quad J_{surf}(\Omega) = \int_\Gamma f(x)\,\mathrm{d}s.$$

These two functions are shape differentiable at Ω and

$$\frac{\partial J_{vol}}{\partial \Omega}(\Omega)(\mathbf{u}) = \int_\Gamma f\,(\mathbf{u}.\mathbf{n})\,\mathrm{d}s \quad \text{and}$$
$$\frac{\partial J_{surf}}{\partial \Omega}(\Omega)(\mathbf{u}) = \int_\Gamma \mathbf{u}.\mathbf{n}\left(\frac{\partial f}{\partial \mathbf{n}} + Hf\right)\mathrm{d}s,$$

for any $\mathbf{u}$ smooth enough, where H is the mean curvature of Γ defined by $H = \nabla.\tilde{\mathbf{n}}$ and $\tilde{\mathbf{n}}$ is the local extension of the normal $\mathbf{n}$ near Γ.

Lemma A.2 (*When the Integrand Depends on the Shape*)**.** *Let us consider a smooth bounded open set $\Omega \in \mathbb{R}^3$ and $f(\Omega, x)$ a smooth function defined in $\mathbb{R}^3$ depending also on the domain. Define*

$$J(\Omega) = \int_\Gamma f(\Omega)\,\mathrm{d}s.$$

This function is shape differentiable at Ω regarding Fréchet and, for any smooth function $\mathbf{u}$, we have:

$$\frac{\partial J}{\partial \Omega}(\Omega)(\mathbf{u}) = \int_\Gamma \left(\frac{\partial f}{\partial \Omega}(\Omega) + \mathbf{u}.\mathbf{n}\left(\frac{\partial f(\Omega)}{\partial \mathbf{n}} + Hf(\Omega)\right)\right)\mathrm{d}s.$$

The next part is intended to give a simple derivation of the Murat–Simon expressions: Lemmas A.1 and A.2, in the two dimensional case.

Appendix B. On a simple derivation of the above announced lemma

Let us start with a two dimensional problem (the boundary is a line)

$$J(\Omega) = \int_\Gamma f(x)\mathrm{d}\ell$$

$\mathrm{d}\ell$ is the curvilinear coordinate, and f is a function which does not depend explicitly on the form, but only on x which is a 2D vector field. Of course x is evaluated at the boundary, since the integral is along the boundary. We have $\mathrm{d}\ell = \mathrm{d}\alpha\sqrt{g}$, where α is a parametrization of a curve (for example if $x(\alpha)$ is parametric representation of a curve, then $g = x'^2$, where prime denotes differentiation with respect to argument). We can thus write

$$J(\Omega) = \int_\Gamma f(x)\sqrt{g}\mathrm{d}\alpha. \tag{29}$$

Since now integration is performed on the parameter α which does not depend on the curve (think of time parametrizing a trajectory!), the variation of J with the shape acquires the simple Euler–Lagrange derivative

$$R \equiv \frac{\delta J}{\delta x} = \frac{\partial(f\sqrt{g})}{\partial x} - \frac{\mathrm{d}}{\mathrm{d}\alpha}\frac{\partial(f\sqrt{g})}{\partial x'}. \tag{30}$$

R is nothing but the functional derivative of J (i.e. $\frac{\delta J}{\delta x}$),[4] but not yet the force (see below). Expliciting out R we have

$$R = \sqrt{g}\frac{\partial}{\partial x}f - f\frac{\mathrm{d}}{\mathrm{d}\alpha}\frac{\partial}{\partial x'}\sqrt{g} - \frac{\mathrm{d}f}{\mathrm{d}\alpha}\frac{\partial\sqrt{g}}{\partial x'}.$$

We have $\partial\sqrt{g}/\partial x' = x'/\sqrt{g}$, $\mathrm{d}/\mathrm{d}\alpha(\sqrt{g}) = x'.x''/\sqrt{g}$, and $\mathrm{d}/\mathrm{d}\alpha(x'/\sqrt{g}) = [x''\sqrt{g} - x'(x'.x'')/\sqrt{g}]/g$. Using the result $r' = \sqrt{g}\mathbf{t}$ (coming from the very definition of the tangent vector $\mathbf{t}$), and $\mathbf{t}' = -H\mathbf{n}\sqrt{g}$, we easily find

$$R = \sqrt{g}\left[Hf\mathbf{n} - \mathbf{t}\frac{\partial f}{\partial \ell} + \frac{\partial f}{\partial x}\right].$$

[3] This is nothing but a Taylor expansion and where $\frac{\partial J}{\partial \Omega}(\Omega)(\mathbf{u})$ can also be alternatively written as $\mathbf{u}.\nabla_\Omega \mathbf{J}(\Omega)$ (this is the shape directional derivative along the displacement direction $\mathbf{u}$).

[4] Note that the relation between the shape derivative used previously and the functional derivative written in this Appendix is $\frac{\partial J}{\partial \Omega}(\Omega)(\mathbf{u}) = \int_\Gamma \mathbf{u}.\mathbf{n}\frac{\delta J}{\delta x}\mathrm{d}\alpha$.

By the definition of the functional derivative we have from (29) and (30)

$$\delta J = \int_\Gamma R\delta x \mathrm{d}\alpha = \int_\Gamma \frac{R}{\sqrt{g}}\delta x \mathrm{d}\ell$$

where δx designates a displacement (or variation) of the shape. The force applies to the real elementary material $\mathrm{d}\ell$ and not to the fictitious parametrization $\mathrm{d}\alpha$. This implies from the above relation that the total force is $R/\sqrt{g}$ (i.e. the quantity which multiplies $\mathrm{d}\ell$ (see also [19,20]). Note that since we confine ourselves to two dimensions, the force is defined per unit length (along the direction along which the membrane is supposed to be translationally invariant).

The force applied on the membrane reads thus (from (30) divided by $\sqrt{g}$ and by noting that $-\mathbf{t}\frac{\partial f}{\partial \ell} + \frac{\partial f}{\partial x}$ defines the normal derivative)

$$\left[Hf\mathbf{n} + \frac{\partial f}{\partial \mathbf{n}}\mathbf{n}\right]$$

since only the normal enters, this means that only normal motion matters. If $\mathbf{u}$ is displacement, the variation with respect to the form acquires the factor $\mathbf{u}.\mathbf{n}$. This is the so-called Murrat-Simon expression (see Lemma A.1). We can reconsider that f depends on shape (actually on x', x'' etc.), we find trivially the generalized expression which contains derivative with respect to form (see Lemma A.2). Extension to 3D is elementary.

Appendix C. The Green formula with surface operators

The Green formula with surface operators is derived in this Appendix. Let any scalar function g and any vector field $\mathbf{v}$ defined over the closed surface Γ, $\mathbf{n}$ is the unit outward normal vector defined as a signed distance function like in the part 2. By (6), we have

$$\int_\Gamma \nabla_s g.\mathbf{v}\mathrm{d}s = \int_\Gamma \nabla g.\mathbf{v}\mathrm{d}s - \int_\Gamma (\nabla g.\mathbf{n})\,(\mathbf{v}.\mathbf{n})\,\mathrm{d}s. \tag{31}$$

We have

$$\int_\Gamma \nabla g.\mathbf{v}\mathrm{d}s = -\int_\Gamma g\nabla.\mathbf{v}\mathrm{d}s + \int_\Gamma \nabla.(g\mathbf{v})\mathrm{d}s. \tag{32}$$

Using (7), (32) gives

$$\int_\Gamma \nabla g.\mathbf{v}\mathrm{d}s = -\int_\Gamma g\nabla_s.\mathbf{v}\mathrm{d}s - \int_\Gamma g\,(\nabla\mathbf{v}.\mathbf{n})\,.\mathbf{n}\mathrm{d}s + \int_\Gamma \nabla.(g\mathbf{v})\mathrm{d}s. \tag{33}$$

By (7), the last term in (33) can be written as

$$\int_\Gamma \nabla.(g\mathbf{v})\mathrm{d}s = \int_\Gamma \nabla_s.(g\mathbf{v})\mathrm{d}s + \int_\Gamma [\nabla(g\mathbf{v})\mathbf{n}]\,.\mathbf{n}\mathrm{d}s. \tag{34}$$

By the Stokes theorem over the closed surface Γ (18),

$$\int_\Gamma \nabla_s.(g\mathbf{v})\mathrm{d}s = \int_\Gamma \nabla_s.[g(\mathbf{v}.\mathbf{n})\mathbf{n}]\,\mathrm{d}s. \tag{35}$$

By (34) and (35)

$$\int_\Gamma \nabla.(g\mathbf{v})\mathrm{d}s = \int_\Gamma (\nabla.\mathbf{n})g\mathbf{v}.\mathbf{n}\mathrm{d}s + \int_\Gamma [\nabla(g\mathbf{v})\mathbf{n}]\,.\mathbf{n}\mathrm{d}s. \tag{36}$$

Using the summation of repeated indices convention, we have:

$$[\nabla(g\mathbf{v})\mathbf{n}]\,.\mathbf{n} = \mathbf{n}_i\mathbf{n}_j\partial_j(g\mathbf{v}_i) = \mathbf{n}_i\mathbf{n}_j g\partial_j\mathbf{v}_i + \mathbf{n}_i\mathbf{n}_j\mathbf{v}_i\partial_j g.$$

Thus,

$$[\nabla(g\mathbf{v})\mathbf{n}]\,.\mathbf{n} = g\,[\nabla\mathbf{v}.\mathbf{n}]\,.\mathbf{n} + (\mathbf{n}.\mathbf{v})(\mathbf{n}.\nabla g). \tag{37}$$

Combining the results (31)–(33), (36) and (37), we obtain

$$\int_\Gamma \nabla_s g.\mathbf{v}\mathrm{d}s + \int_\Gamma g\nabla_s.\mathbf{v}\mathrm{d}s - \int_\Gamma g(\nabla.\mathbf{n})\mathbf{v}.\mathbf{n}\mathrm{d}s = 0.$$

References

[1] U. Seifert, Configurations of fluid membranes and vesicles, Adv. Phys. 46 (1997) 13–137.
[2] S.A. Safran, Statistical Thermodynamics of Surfaces, Interfaces and Membranes, in: Frontier in Physics, vol 90, Addison-Wesley Publishing Company, Reading, MA, 1994.
[3] P.M. Vlahovska, T. Podgorski, C. Misbah, Vesicles and red blood cells in flow: from individual dynamics to rheology, C. R. Physique 10 (2009) 775–789.
[4] O.-Y. Zhong-can, W. Helfrich, Bending energy of vesicle membranes: general expressions for the first, second and third variation of the shape energy and applications to spheres and cylinders, Phys. Rev. A 39 (10) (1989) 5280–5288.
[5] R. Capovilla, J. Guven, Stresses in lipid membranes, J. Phys. A: Math. Gen. 35 (2002) 6233–6247.
[6] D.A. Edwards, H. Brenner, D.T. Wasan, Interfacial Transport Processes and Rheology, Butterworth-Heinemann, Boston, MA, 1991.
[7] J. Simon, Differentiation with respect to the domain in boundary value problems, J. Numer. Funct. Anal. Optim. 2 (7–8) (1980) 649–687.
[8] T. Biben, K. Kassner, C. Misbah, Phase-field approach to three-dimensional vesicle dynamics, Phys. Rev. E 72 (2005) 041921.
[9] T. Milcent, Une approche eulérienne du couplage fluide-structure, analyse mathématique et applications en biomécanique, Ph.D. Thesis, Université J. Fourier, Grenoble, France, 2009.
[10] T. Milcent, Comparison between shape optimization and volumic level set approximation for geometrical functionals, arXiv:0806.1288.
[11] E. Maitre, C. Misbah, P. Peyla, A. Raoult, Comparison between advected-field and level-set methods in the study of vesicle dynamics, 2009 (unpublished), arXiv:1005.4120v1.
[12] D. Jamet, C. Misbah, Toward a thermodynamically consistent picture of the phase-field model of vesicles: Curvature energy, Phys. Rev. E 78 (2008) 031902.
[13] S. Leibler, in: D.R. Nelson, T. Piran, S. Weinberg (Eds.), Statistical Mechanics of Surfaces and Membranes, World Scientific, Singapore, 1989.
[14] R.G. Larson, The Structure and Rheology of Complex Fluids, Oxford University Press, Oxford, UK, 1999.
[15] F. Divet, G. Danker, C. Misbah, Fluctuations and instability of a biological membrane induced by interaction with macromolecules, Phys. Rev. E 73 (2002) 041901–041914.
[16] F. Campelo, A. Hernandez-Machado, Model for curvature-driven pearling instability in membranes, Phys. Rev. Lett. 99 (8) (2007) 088101.
[17] G. Allaire, F. Jouve, Minimum stress optimal design with the level set method, Int. J. Boundary Elements Appl. (in press).
[18] F. Murat, J. Simon, Quelques résultats sur le contrôle par un domaine géométrique, Tech. Rep. LA 189, Lab. d'Analyse Numérique, Univ. Paris VI, 1974.
[19] W. Cai, T.C. Lubensky, Hydrodynamics and dynamic fluctuations of fluid membranes, Phys. Rev. E 52 (4) (1995) 4251–4266.
[20] B. Kaoui, G. Ristow, I. Cantat, C. Misbah, W. Zimmermann, Lateral migration of a 2d vesicle in unbounded poiseuille flow, Phys. Rev. E 77 (2008) 021903.